Amherst, NY

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What Do Biomedical Terminologies Tell Us About Biomedicine?

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Outline

- Why biomedical terminologies?
- Introduction to biomedical terminologies through an example
- Biomedical terms as names for biomedical classes
- Terminological relations as a surrogate for ontological relations

Why biomedical terminologies?

Why biomedical terminologies?

- To support a theory of diseases
- To classify diseases
- To support epidemiology
- To index and retrieve information
- To serve as a reference

To support a theory of diseases

- Hippocrates
  - Dismisses superstition
  - Four humors
    - Blood
    - Phlegm
    - Yellow bile
    - Black bile
- Thomas Sydenham (1624-1689)
  - *Medical observations on the history and cure of acute diseases* (1676)

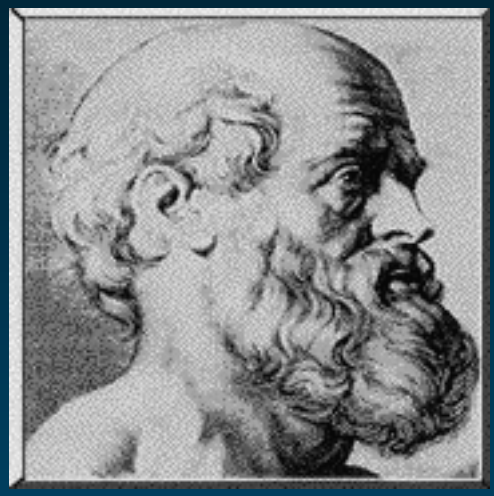
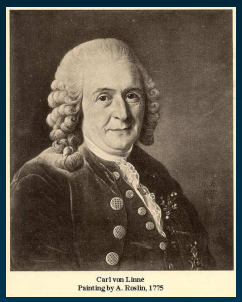
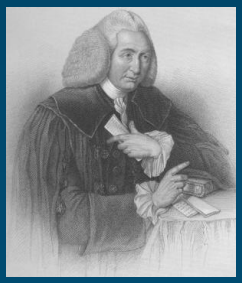


Figure 36 Thomas Sydenham (1624–1689)

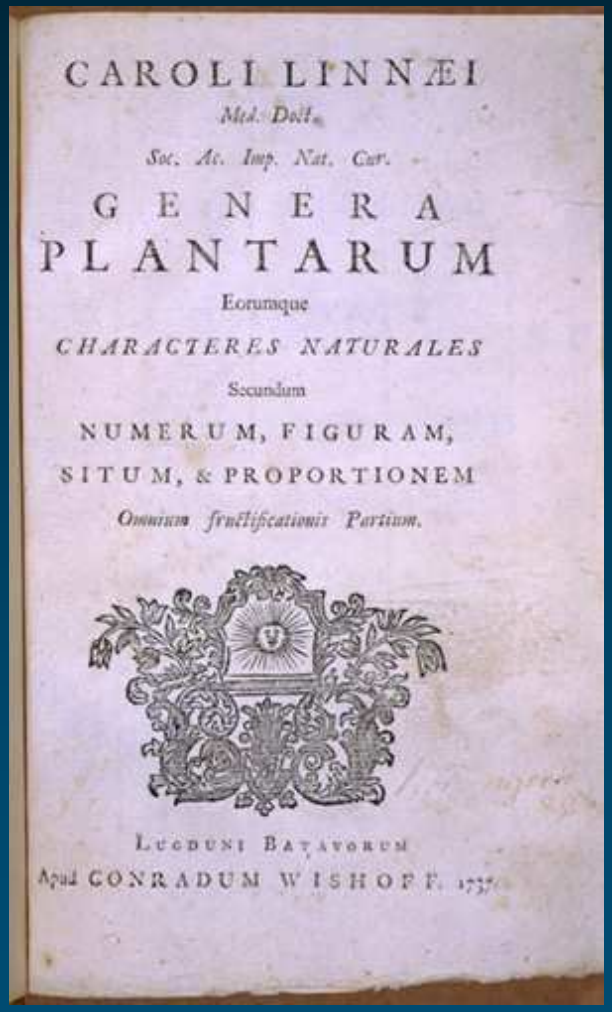
To classify diseases (and plants)

- Carolus Linnaeus (1707-1778)
  - *Genera Plantarum* (1737)
  - *Genera Morborum* (1763)
- François Boissier de La Croix a.k.a. F. B. de Sauvages (1706-1767)
  - *Methodus Foliorum* (1751)
  - *Nosologia Methodica* (1763/68)
- William Cullen (1710-1790)
  - *Synopsis Nosologiae Methodicae* (1785)





From plants…



CAROLI LINNÆI

Med. Doct.

Soc. Ac. Imp. Nat. Cur.

GENERA PLANTARUM

Eorumque

CHARACTERES NATURALES

Secundum

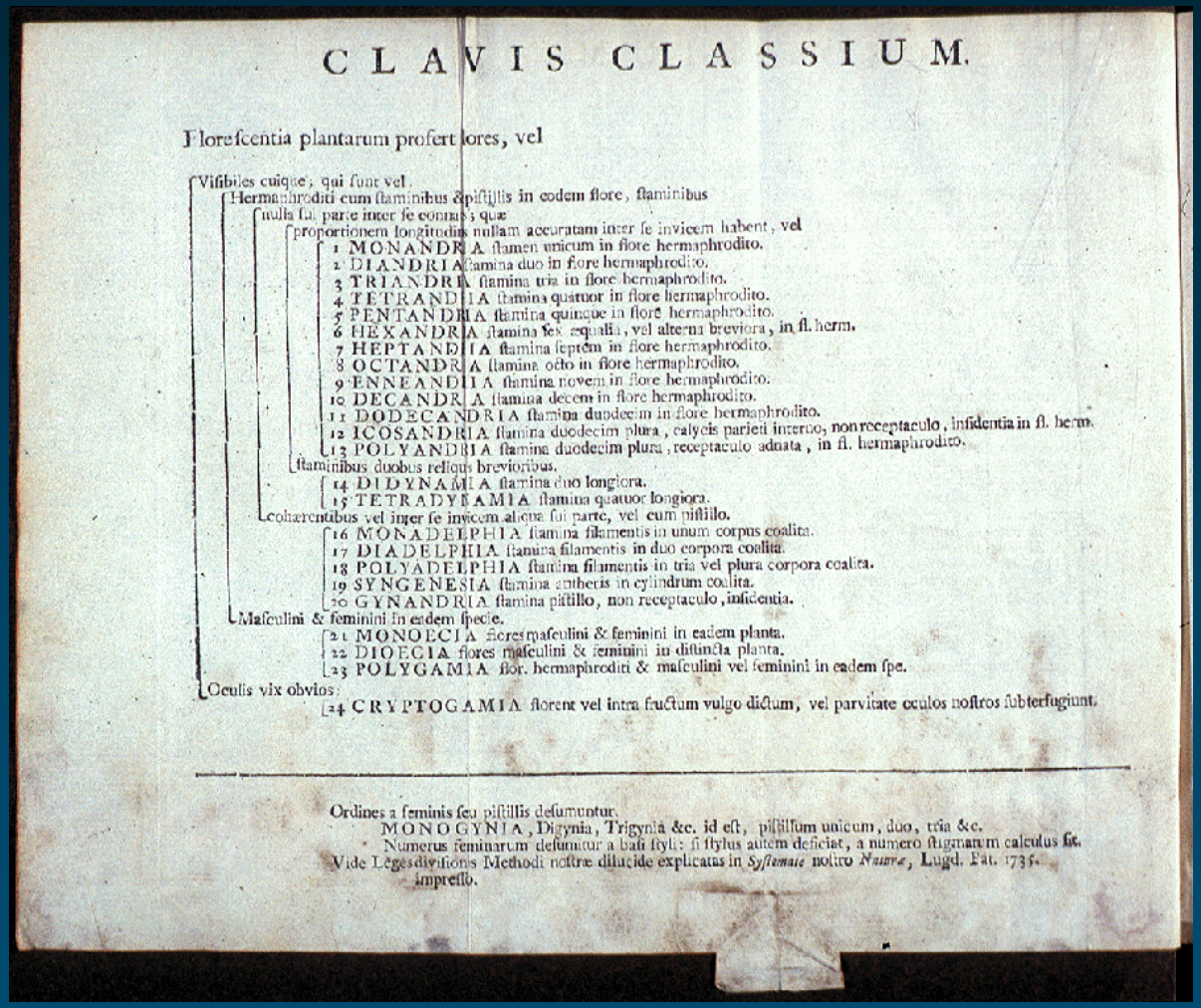
NUMERUM, FIGURAM,

SITUM, & PROPORTIONEM

Omnium fructificationis Partium.

LUGDUNI BATAVORUM

Apud CONRADUM WISHOFF. 1737.



CLAVIS CLASSIUM.

Floreſcentia plantarum profert flores, vel

- Viſibiles cuique; qui ſunt vel.
  - Hermaphroditi cum ſtaminibus & piſtillis in eodem flore, ſtaminibus
    - nulla ſui parte inter ſe connatis; quæ
      - proportionem longitudinis nullam accuratam inter ſe invicem habent, vel
        1. MONANDRIA ſtamen unicum in flore hermaphrodito.
        2. DIANDRIA ſtamina duo in flore hermaphrodito.
        3. TRIANDRIA ſtamina tria in flore hermaphrodito.
        4. TETRANDRIA ſtamina quatuor in flore hermaphrodito.
        5. PENTANDRIA ſtamina quinque in flore hermaphrodito.
        6. HEXANDRIA ſtamina ſex æqualia, vel alterna breviora, in fl. herm.
        7. HEPTANDRIA ſtamina ſeptem in flore hermaphrodito.
        8. OCTANDRIA ſtamina octo in flore hermaphrodito.
        9. ENNEANDRIA ſtamina novem in flore hermaphrodito.
        10. DECANDRIA ſtamina decem in flore hermaphrodito.
        11. DODECANDRIA ſtamina duodecim in flore hermaphrodito.
        12. ICOSANDRIA ſtamina duodecim plura, calycis parieti interno, non receptaculo, inſidentia in fl. herm.
        13. POLYANDRIA ſtamina duodecim plura, receptaculo adnata, in fl. hermaphrodito.
      - ſtaminibus duobus reliquis brevioribus.
        14. DIDYNAMIA ſtamina duo longiora.
        15. TETRADYNAMIA ſtamina quatuor longiora.
    - cohærentibus vel inter ſe invicem aliqua ſui parte, vel cum piſtillo.
      16. MONADELPHIA ſtamina filamentis in unum corpus coalita.
      17. DIADELPHIA ſtamina filamentis in duo corpora coalita.
      18. POLYADELPHIA ſtamina filamentis in tria vel plura corpora coalita.
      19. SYNGENESIA ſtamina antheris in cylindrum coalita.
      20. GYNANDRIA ſtamina piſtillo, non receptaculo, inſidentia.
  - Maſculini & feminini in eadem ſpecie.
    21. MONOECIA flores maſculini & feminini in eadem planta.
    22. DIOECIA flores maſculini & feminini in diſtincta planta.
    23. POLYGAMIA flor. hermaphroditi & maſculini vel feminini in eadem ſpe.
- Oculis vix obvios:
  24. CRYPTOGAMIA florent vel intra fructum vulgo dictum, vel parvitate oculos noſtros ſubterfugiunt.

Ordines a feminis ſeu piſtillis deſumuntur.
MONOGYNIA, Digynia, Trigynia &c. id eſt, piſtillum unicum, duo, tria &c.
Numerus feminarum deſumitur a baſi ſtyli: ſi ſtylus autem deficiat, a numero ſtigmatum calculus ſit.
Vide Leges divifionis Methodi noſtræ dilucide explicatas in *Syſtemate* noſtro *Naturæ*, Lugd. Bat. 1735.
impreſſo.

… to diseases

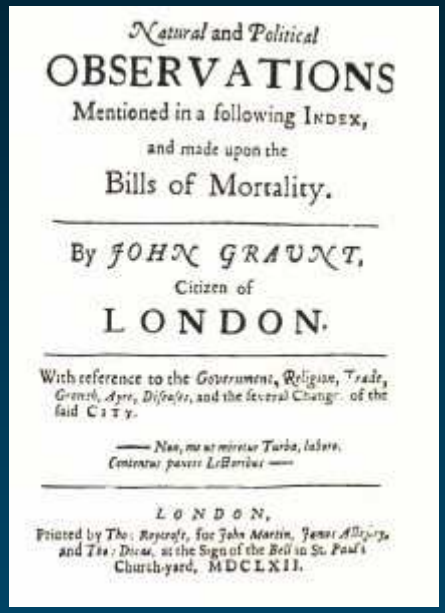
- Four categories (W. Cullen)
  - Fevers
  - Nervous disorders
  - Cachexias
  - Local diseases

"The distinction of the genera of diseases, the distinction of the species of each, and often even that of the varieties, I hold to be a necessary foundation of every plan of physic, whether dogmatical or empirical."
– William Cullen, Edinburgh, 1785
Synopsis Nosologia Methodicae

(Cited by Chris Chute)

To support epidemiology

- John Graunt (1620-1674)
  - Analyzes the vital statistics of the citizens of London
- William Farr (1807-1883)
  - Medical statistician
  - Improves Cullen's classification
  - Contributes to creating ICD
- Jacques Berthillon (1851-1922)
  - Chief of the statistical services (Paris)
  - Classification of causes of death (161 rubrics)



Natural and *Political*

OBSERVATIONS

Mentioned in a following INDEX,

and made upon the

Bills of Mortality.

By JOHN GRAUNT,

Citizen of

LONDON.

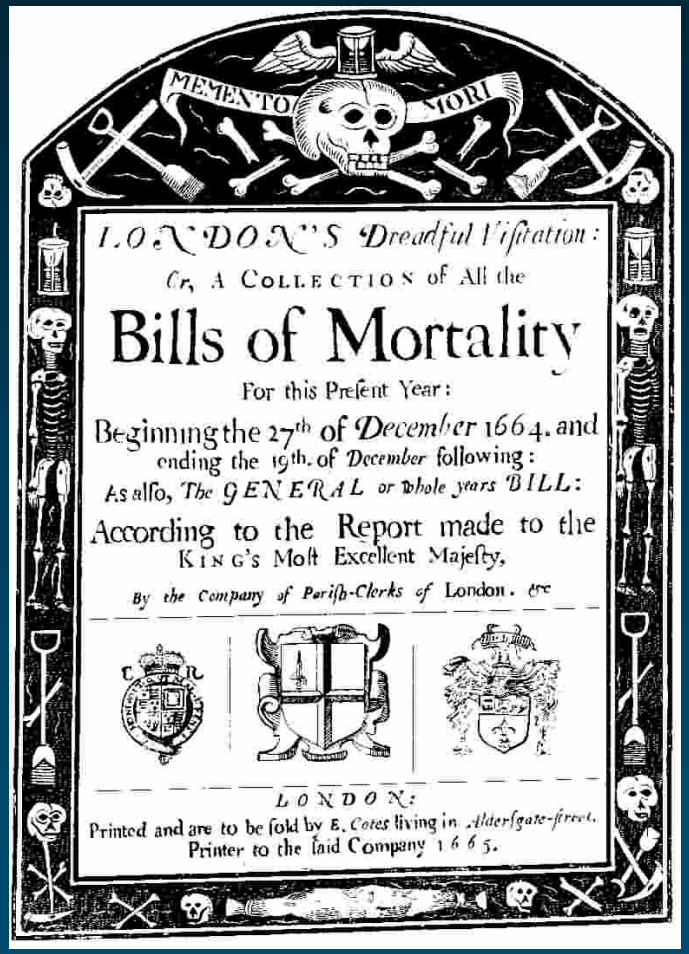
With reference to the *Government*, *Religion*, *Trade*, *Growth*, *Ayre*, *Diseases*, and the several Changes of the said CITY.

—— *Nec, me ut miretur Turba, laboro,*
Contentus paucis Lectoribus ——

LONDON,

Printed by *Tho: Roycroft*, for *John Martin*, *James Allestry*, and *Tho: Dicas*, at the Sign of the *Bell* in St. *Paul's* Church-yard, MDCLXII.

London Bills of Mortality



A generall Bill for this present year, ending the 19 of *December* 1665. according to the Report made to the KINGS most Excellent Majest..

By the Company of Parish Clerks of *London*, &c.

The Diseases and Casualties this year.

Abortive and Stillborne	617	Executed	21	Palsie	50
Aged	1545	Flox and Small Pox	655	Plague	68596
Ague and Feaver	5257	Found dead in Streets, fields, &c.	2	Planet	6
Appoplex and Suddenly	116	French Pox	86	Pleurisie	15
Bedrid	12	Frighted	23	Poysoned	1
Blasted	5	Gout and Sciatica	27	Quinsie	35
Bleeding	16	Grief	46	Rickets	557
Bloody Flux, Scowring & Flux	185	Griping in the Guts	1288	Rising of the Lights	549
Burnt and Scalded	8	Hanged & made away themselves	7	Rupture	34
Calenture	3	Headmouldshot & Mouldfallen	14	Scurvy	17
Cancer, Gangrene and Fistula	56	Jaundies	100	Shingles and Swine pox	2
Canker, and Thrush	111	Impostume	227	Sores, Ulcers, broken and bruised	
Childbed	625	Kild by severall accidents	46	Limbs	82
Chrisomes and Infants	1258	Kings Evill	88	Spleen	14
Cold and Cough	65	Leprosie	2	Spotted Feaver and Purples	1929
Collick and Winde	134	Lethargy	14	Stopping of the Stomach	334
Consumption and Tisick	4808	Livergrown	21	Stone and Strangury	98
Convulsion and Mother	2036	Meagrom and Headach	82	Suddat	222
Distracted	5	Measles	7	Teeth and Worms	2614
Dropsie and Tympany	1478	Murthered and Shot	9	Vomiting	54
Drowned	53	Overlaid & Starved	45	Worm	7

Christened	Males	5114	Buried	Males 48568
	Females	4853		Females 48737
	In all	9967		In all 97305

Of the Plague 68596

Increased in the Burials in the 130 Parishes and at the Pest-house this year 79029

Increased of the Plague in the 130 Parishes and at the Pest-houses this year 68590

Limitations of existing classifications

"The advantages of a uniform statistical nomenclature, however imperfect, are so obvious, that it is surprising no attention has been paid to its enforcement in Bills of Mortality. Each disease has, in many instances, been denoted by three or four terms, and each term has been applied to as many different diseases: vague, inconvenient names have been employed, or complications have been registered instead of primary diseases. The nomenclature is of as much importance in this department of inquiry as weights and measures in the physical sciences, and should be settled without delay."

– William Farr

First annual report.

London, Registrar General of England and Wales, 1839, p. 99.

To index and retrieve information

- Biomedical literature
  - MEDLINE (15M citations from 4600 journals)
  - Manually indexed
  - Medical Subject Headings (MeSH)
- Genome
  - Model organism databases (Fly, Mouse, Yeast, …)
  - Manually / semi-automatically curated
  - Gene Ontology

MEDLINE and MeSH

☐ **1:** J Hist Neurosci. 2004 Mar;13(1):91-101. Related Articles, Links

MetaPress

Black bile and psychomotor retardation: shades of melancholia in Dante's Inferno.

Widmer DA.

Memorial Sloan-Kettering Cancer Center, New York, NY 10017, USA. widmerd@mskcc.org

The history of melancholy depression is rich with images of movement retardation and mental dysfunction. The recent restoration of psychomotor symptoms to the diagnostic terminology of affective disorder is not novel to the students of medieval melancholia. The move back to the biology of this psychomotor dysfunction with the technical advances in brain imaging in recent years only echoes centuries-old writings on the centrality of movement changes in the depressive condition. The Inferno, the first cantica of Dante Alighieri's Commedia, has a wonderful abundance of allusions to the importance of psychomotor symptoms in describing the depressed individual. Slowed steps, garbled speech, frozen tears, these and many other images keep the physical manifestations of psychomotor suffering in the forefront of the reader's mind. Considering Medieval and Renaissance writings on melancholy suffering, it is fitting that Dante shows a bodily illness reflected in the hellish torments visited on the damned. From the souls of the sullen to those of the violent, the panorama of psychomotor symptoms plays a prominent role in the poem as well as in the medical and literary prose of succeeding centuries.

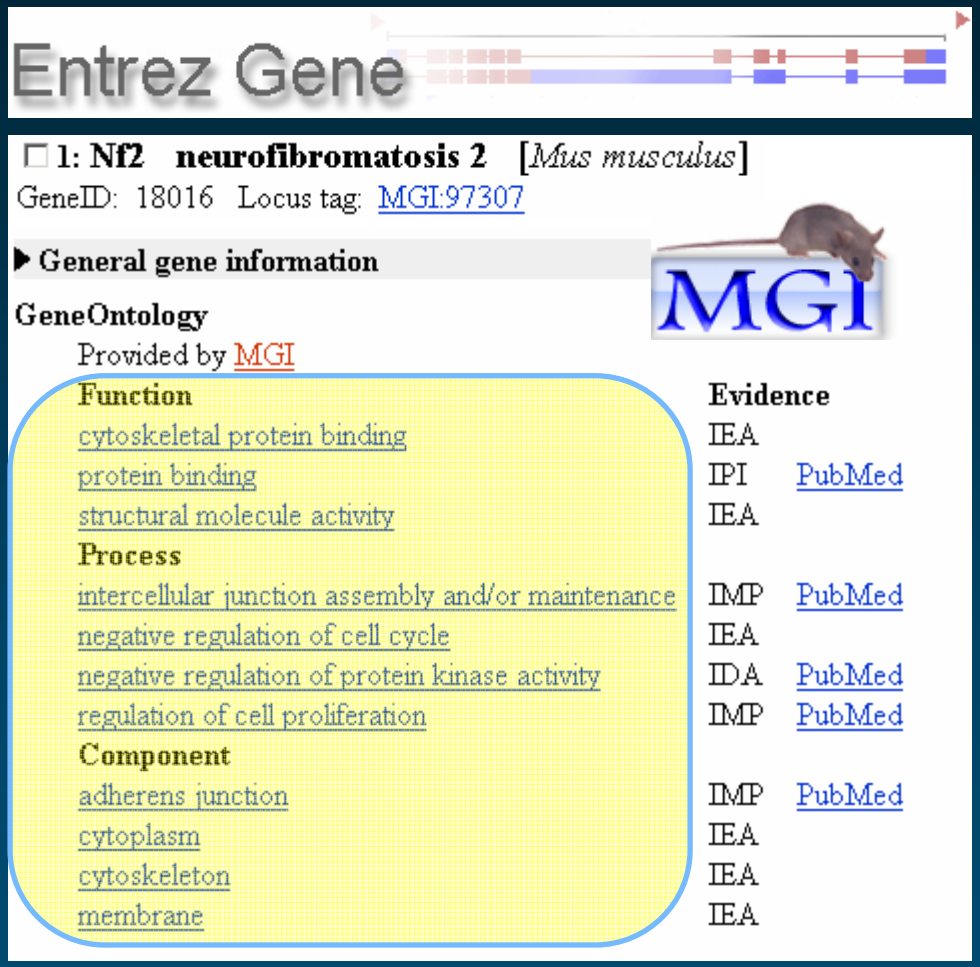
MeSH Terms:

- Depressive Disorder/history*
- History of Medicine, Medieval
- Human
- Italy
- Literature, Medieval/history*
- Medicine in Literature*
- Poetry/history*
- Psychomotor Disorders/history*

PubMed

National Library of Medicine NLM

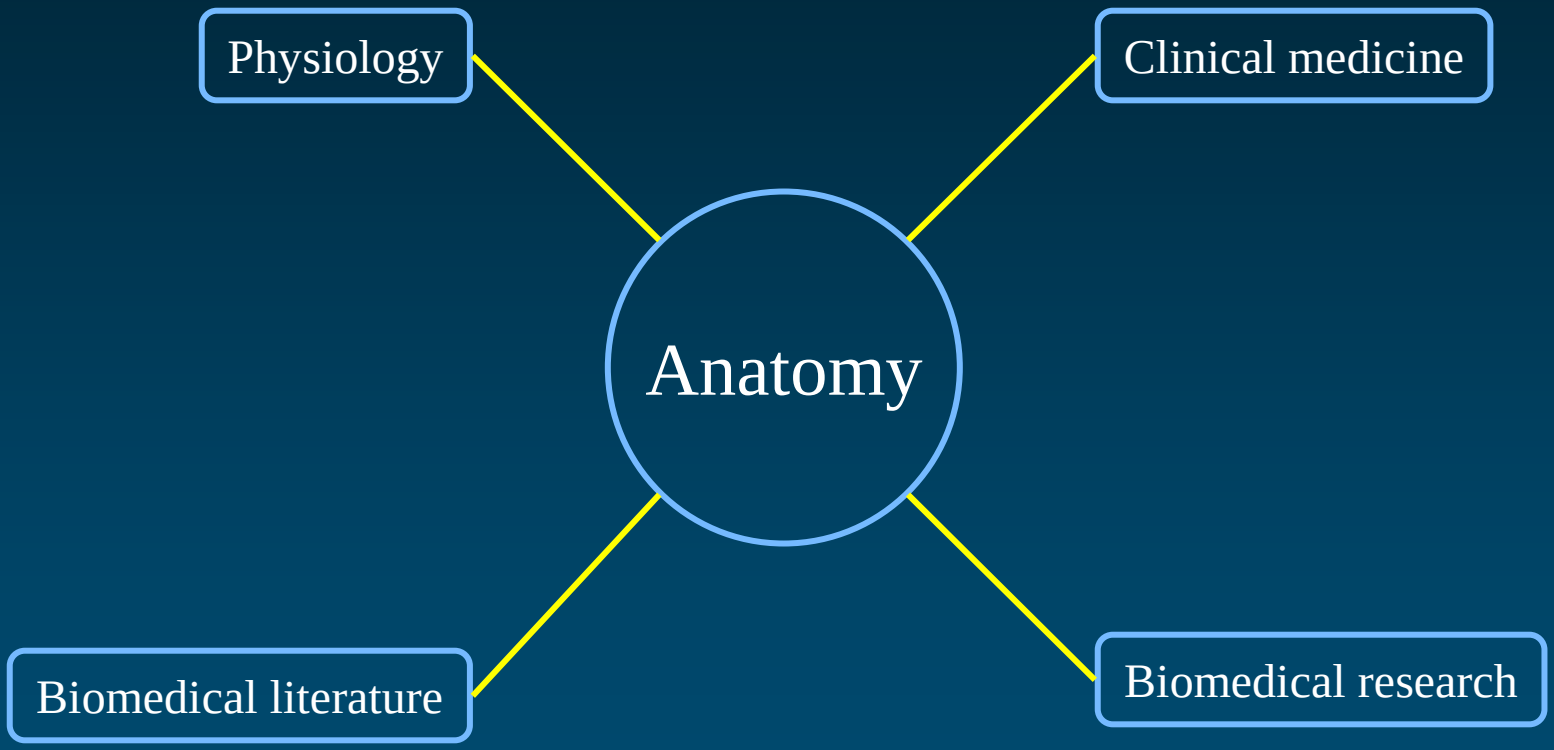
Mouse Genome Database and GO



To serve as a reference

- Reference terminology/ontology
  - Universally needed
  - Developed independently of any purposes
  - Reusable by many applications
- Examples
  - VA National Drug File (NDF)
  - Foundational Model of Anatomy (FMA)
  - SNOMED CT

Anatomy in Biomedicine

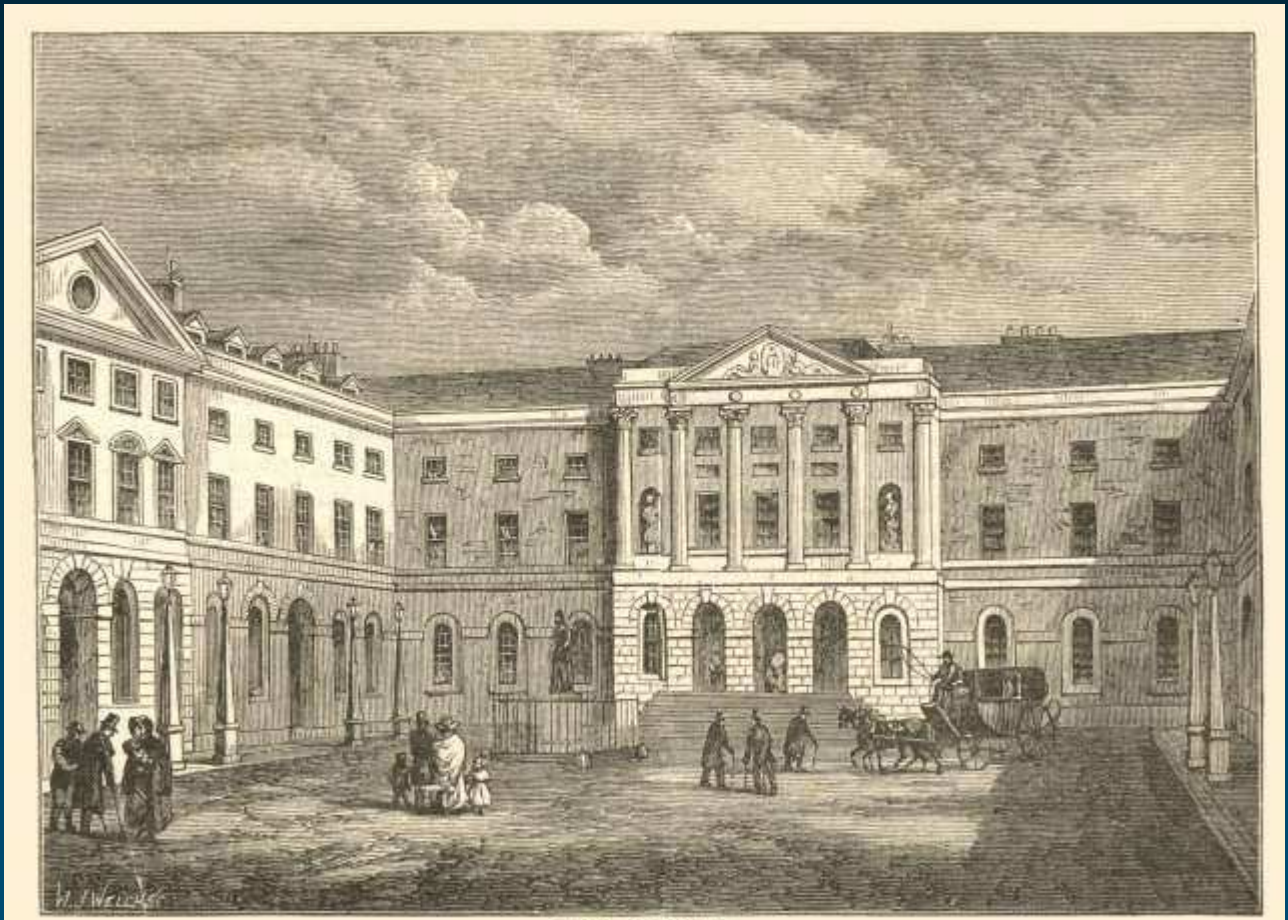


Administrative terminologies

- Coding patient records
  - International Classification of Primary Care (ICPC)
  - SNOMED
  - Read Codes
- Reporting claims to health insurance companies
  - Current Procedural Terminology (CPT)
  - International Classification of Diseases (ICD-9 CM)
  - Healthcare Common Procedure Coding System (HCPCS)

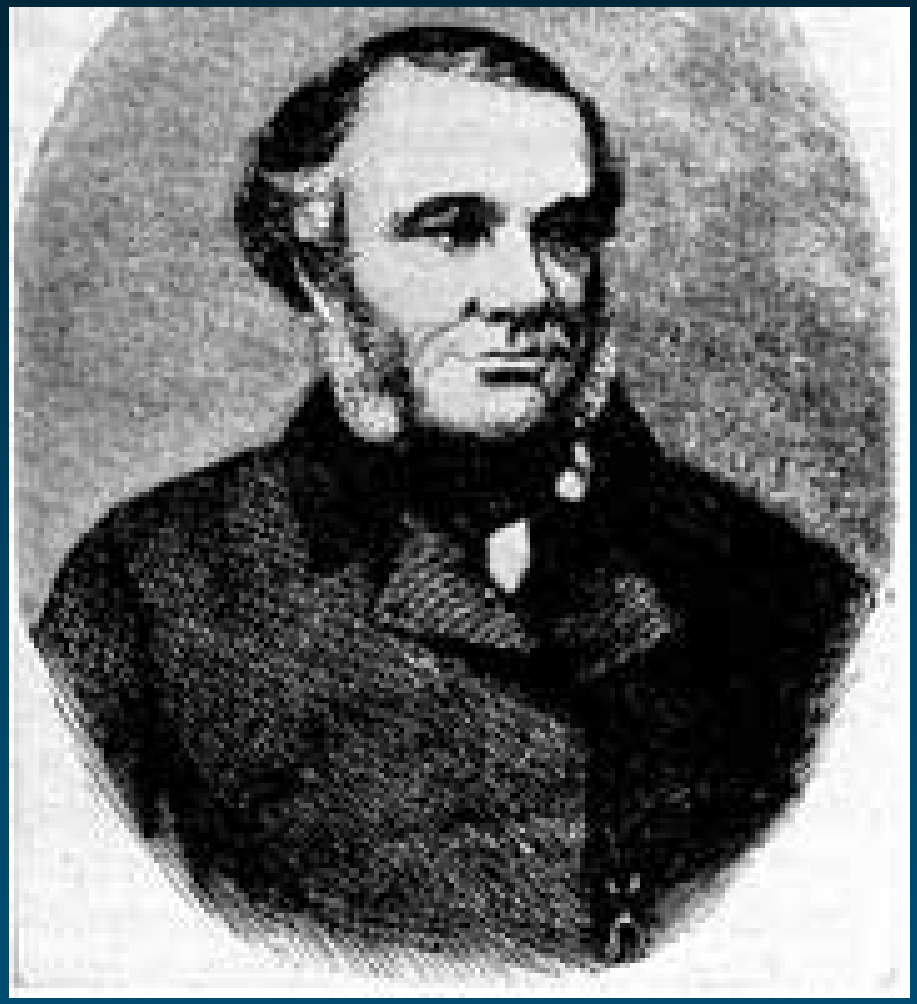
Introduction to biomedical terminologies through an example

Guy's Hospital, London



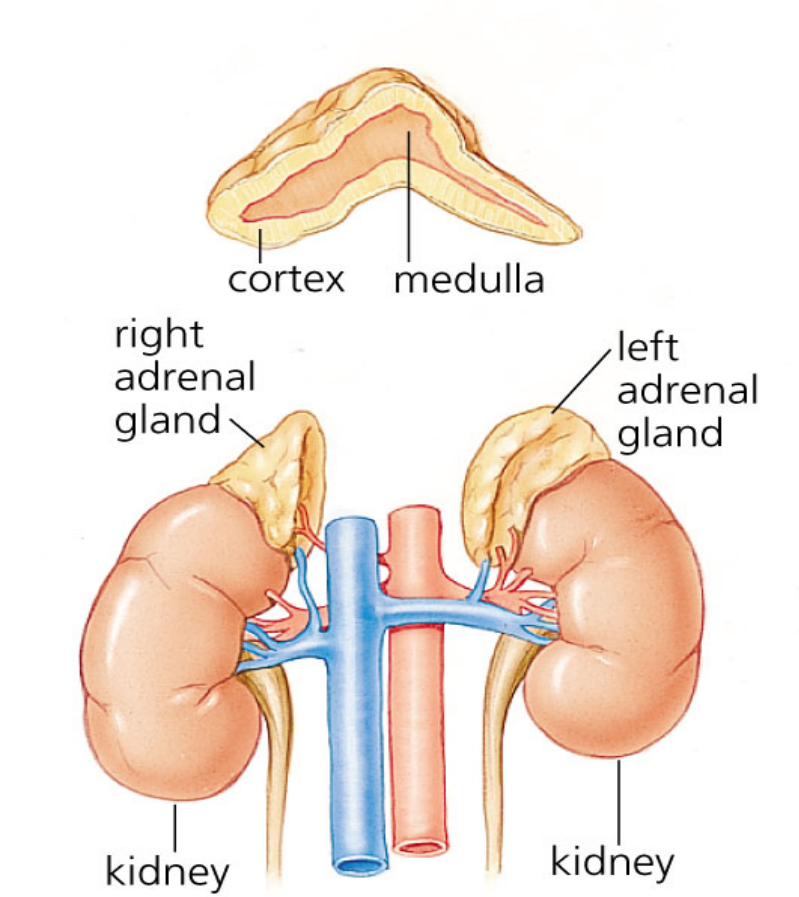
GUY'S HOSPITAL.

Thomas Addison (1795-1860)



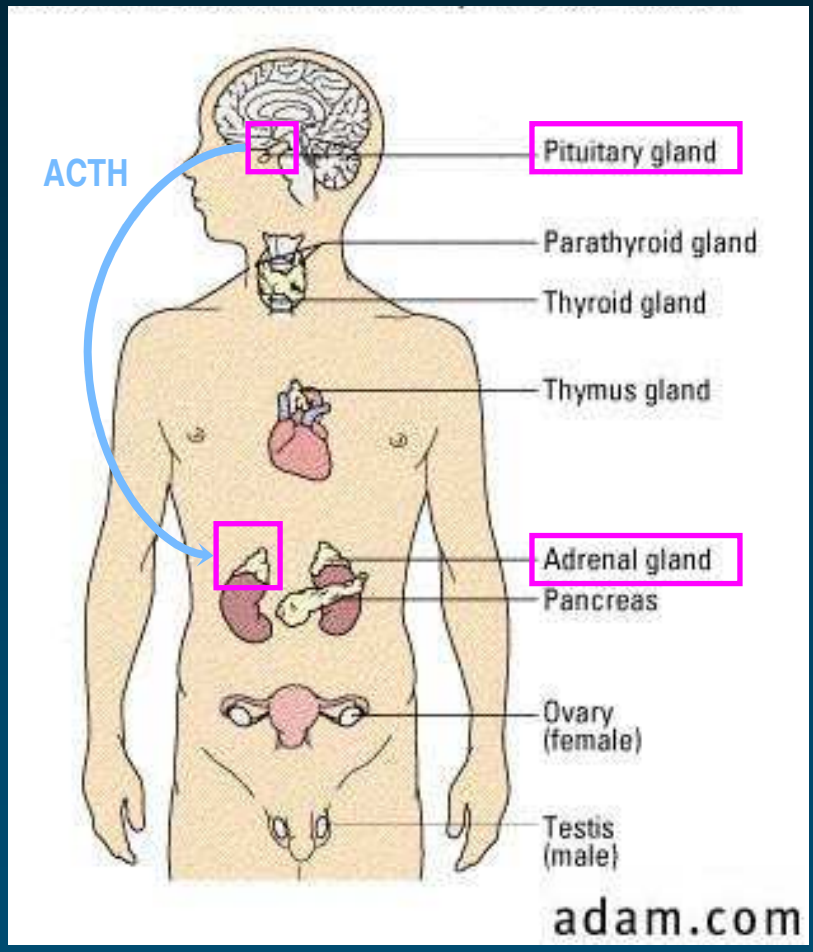
Addison’s disease

- Addison's disease is a rare endocrine disorder
- Addison's disease occurs when the adrenal glands do not produce enough of the hormone cortisol
- For this reason, the disease is sometimes called chronic adrenal insufficiency, or hypocortisolism



Adrenal insufficiency Clinical variants

- Primary / Secondary
  - Primary: lesion of the adrenal glands themselves
  - Secondary: inadequate secretion of ACTH by the pituitary gland
- Acute / Chronic
- Isolated / Polyendocrine deficiency syndrome



Addison's disease: Symptoms

- Fatigue
- Weakness
- Low blood pressure
- Pigmentation of the skin (exposed and non-exposed parts of the body)
- …

AD in medical vocabularies

- Synonyms: different terms
  - Addisonian syndrome — eponym
  - Bronzed disease — symptoms
  - Addison melanoderma — symptoms
  - Asthenia pigmentosa — symptoms
  - Primary adrenal deficiency — clinical variants
  - Primary adrenal insufficiency — clinical variants
  - Primary adrenocortical insufficiency — clinical variants
  - Chronic adrenocortical insufficiency — clinical variants
- Contexts: different hierarchies

Internal Classification of Diseases

CHAPTER 4

Endocrine, nutritional and metabolic diseases (E00-E90)

Disorders of other endocrine glands (E20-E35)

E27 Other disorders of adrenal gland

E27.0 Other adrenocortical overactivity
Overproduction of ACTH, not associated with Cushing's disease
Premature adrenarche
Excludes1: Cushing's syndrome (E24.-)

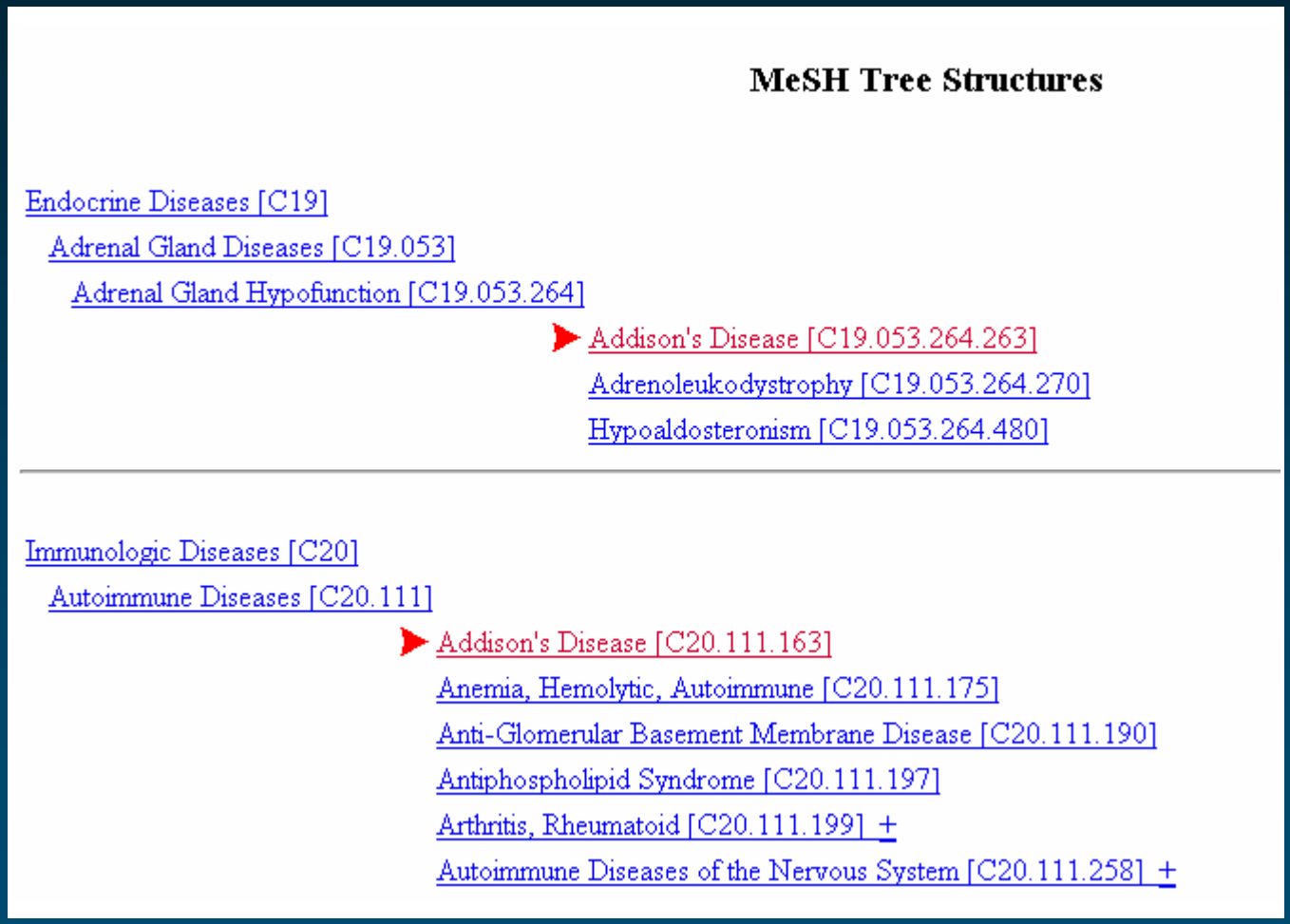
E27.1 Primary adrenocortical insufficiency
Addison's disease
Adrenocortical insufficiency NOS
Autoimmune adrenalitis
Excludes1: Addison only phenotype adrenoleukodystrophy (E71.428)
amyloidosis (E85)
tuberculous Addison's disease (A18.7)
Waterhouse-Friderichsen syndrome (A39.1)

E27.2 Addisonian crisis
Adrenal crisis
Adrenocortical crisis

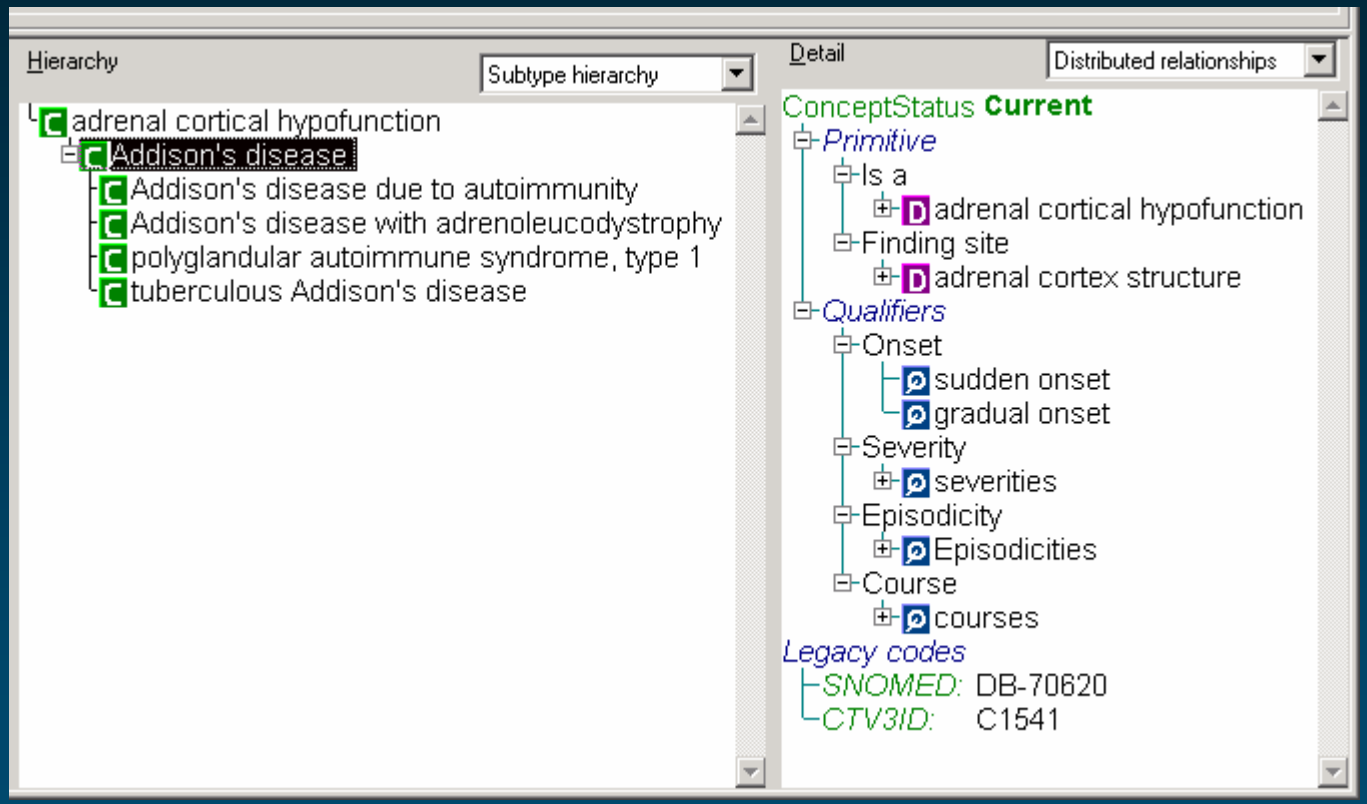
E27.3 Drug-induced adrenocortical insufficiency
Code first (T36-T50) to identify drug

E27.4 Other and unspecified adrenocortical insufficiency

Medical Subject Headings



SNOMED CT


Hierarchy
Subtype hierarchy
adrenal cortical hypofunction
Addison's disease
Addison's disease due to autoimmunity
Addison's disease with adrenoleucodystrophy
polyglandular autoimmune syndrome, type 1
tuberculous Addison's disease
Detail
Distributed relationships
ConceptStatus Current
Primitive
Is a
adrenal cortical hypofunction
Finding site
adrenal cortex structure
Qualifiers
Onset
sudden onset
gradual onset
Severity
severities
Episodicity
Episodicities
Course
courses
Legacy codes
SNOMED: DB-70620
CTV3ID: C1541

Biomedical terms as names for biomedical classes

Terms reflecting valid classes

- Pulmonary anthrax
- BRCA1 protein
- Coronary artery
- Coronary artery bypass
- …

- Non-insulin dependent diabetes mellitus
- Non-Hodgkin lymphoma
- Non-steroidal anti-inflammatory drugs
- Non-opioid analgesics
- Non-invasive medical procedure

Issues

- Multiple terms for a class
- Multiple classes for a term
- Presence of non-ontological features in terms
- Composite terms

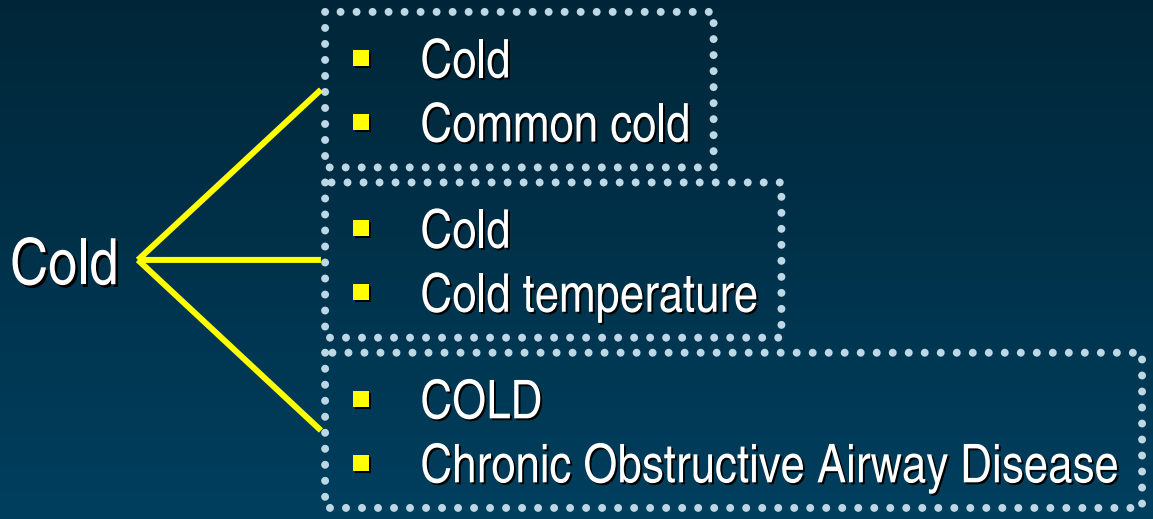
Multiple terms for a class

- Synonymy
  - Left coronary artery
  - LCA
  - Arteria coronaria sinistra
  - Addison's disease
  - Primary adrenocortical insufficiency
- "Clinical synonymy" (vs. identity)
  - Abdominal swelling
  - Swollen abdomen
  - Posttransfusion hepatitis
  - Posttransfusion viral hepatitis
  - Addison's disease
  - Primary adrenocortical insufficiency

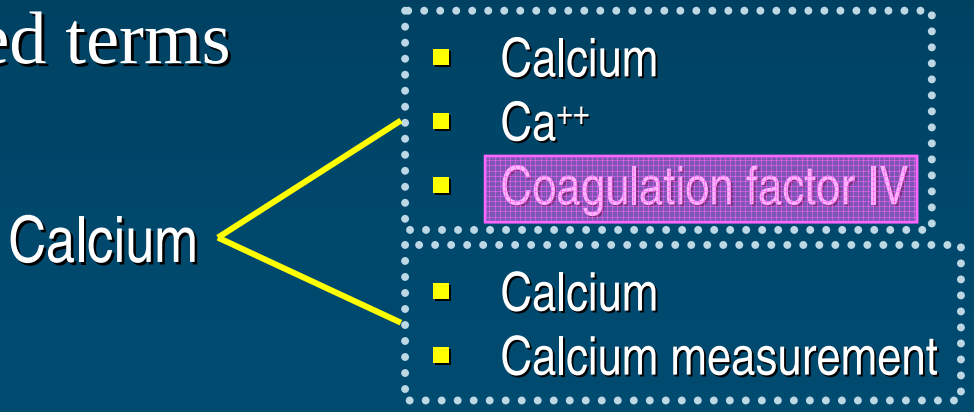
vs. Waterhouse-Friderichsen Syndrome

Multiple classes for a term

- Polysemy



- Truncated terms



Non-ontological features in terms

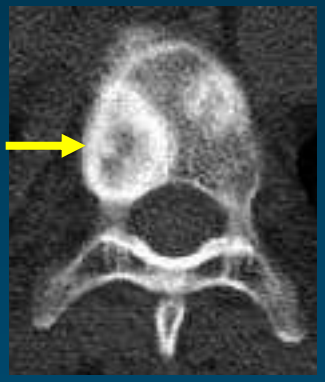
- Epistemological features
  - Gallbladder calculus without mention of cholecystitis
  - Diarrhea of presumed infectious origin
  - Replacement of unspecified heart valve
  - …

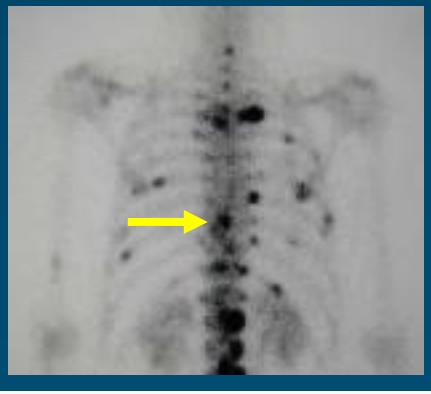
Ontology vs. Epistemology

- Ontology
  - Invariants in reality
    - Classes (universals)
    - Relations between them
  - Theory of reality

- Epistemology
  - Knowledge about such entities
  - Perception of reality

Bone metastasis





Bone metastasis
diagnosed by CT scan

Bone metastasis
diagnosed by Tc99m bone scintiscan

Composite terms

- Sentence-like terms
  - Several classes and their relations
  - May contain epistemological features
- Tuberculosis of adrenal glands, tubercle bacilli not found (in sputum) by microscopy, but found by bacterial culture

More composite terms

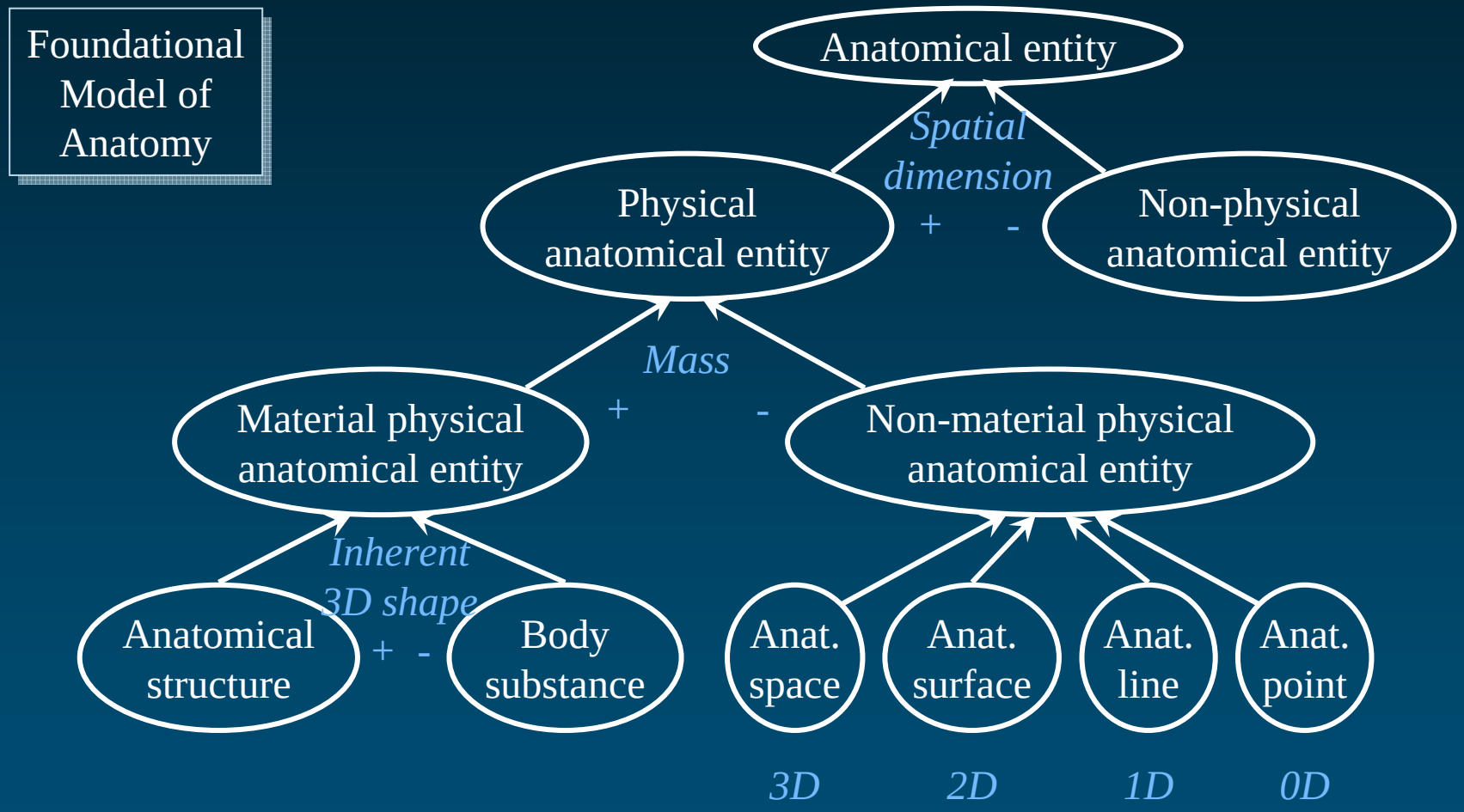
- Nontraffic accident involving being accidentally pushed from motor vehicle, except off-road motor vehicle, while in motion, not on public highway, driver of motor vehicle injured
- Determine whether the elder patient and caretaker have a functional social support network to assist the patient in performing activities of daily living and in obtaining health care, transportation, therapy, medications, community resource information, financial advice, and assistance with personal problems
- Telephone call by a physician to patient or for consultation or medical management or for coordinating medical management with other health care professionals (eg, nurses, therapists, social workers, nutritionists, physicians, pharmacists); complex or lengthy (eg, lengthy counseling session with anxious or distraught patient, detailed or prolonged discussion with family members regarding seriously ill patient, lengthy communication necessary to coordinate complex services of several different health professionals working on different

Terminological relations as a surrogate for ontological relations

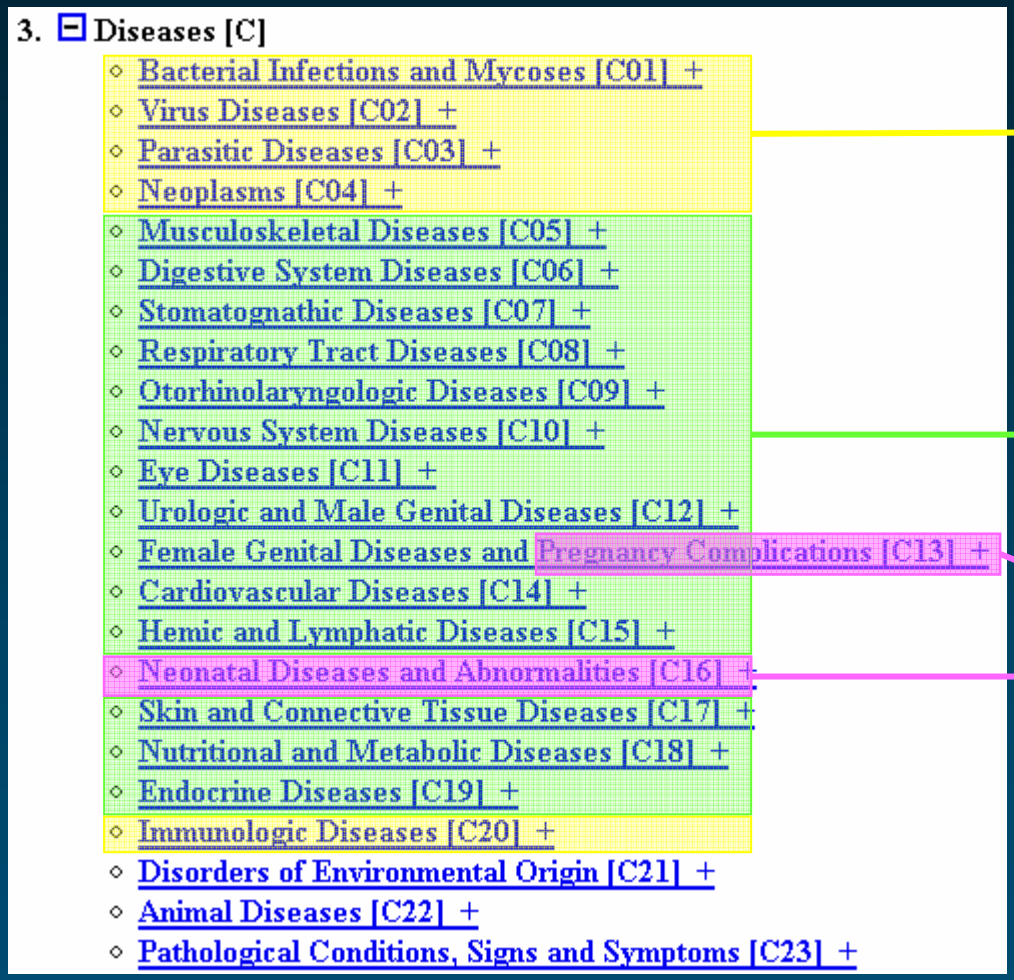
Issues

- Lack of explicit classificatory principle
- Underspecification of the relations
- Thesaurus relations
- Limited depth in hierarchies “by design”

Explicit classificatory principle



No explicit classificatory principle



agent/cause

location

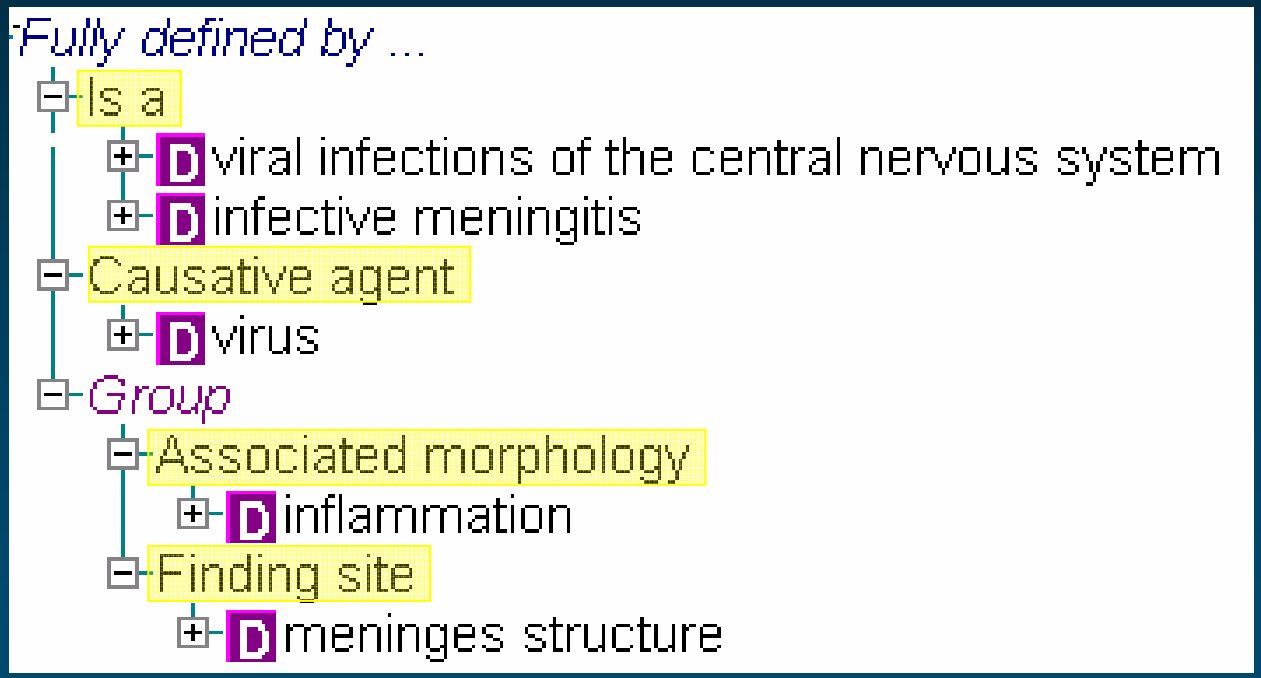
stage in life

1. Certain infectious and parasitic diseases
2. Neoplasms
3. Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism
4. Endocrine, nutritional, and metabolic diseases
5. Mental and behavioral disorders
6. Diseases of nervous system
7. Diseases of the eye and adnexa
8. Diseases of the ear and mastoid process
9. Diseases of circulatory system
10. Diseases of respiratory system
11. Diseases of digestive system
12. Diseases of the skin and subcutaneous tissue
13. Diseases of the musculoskeletal system and connective tissue
14. Diseases of the genitourinary system
15. Pregnancy, childbirth, and the puerperium
16. Certain conditions originating in the newborn (perinatal) period
17. Congenital malformations, deformations and chromosomal abnormalities
18. Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified
19. Injury, poisoning and certain other consequences of external causes
20. External causes of morbidity
21. Factors influencing health status and contact with health service

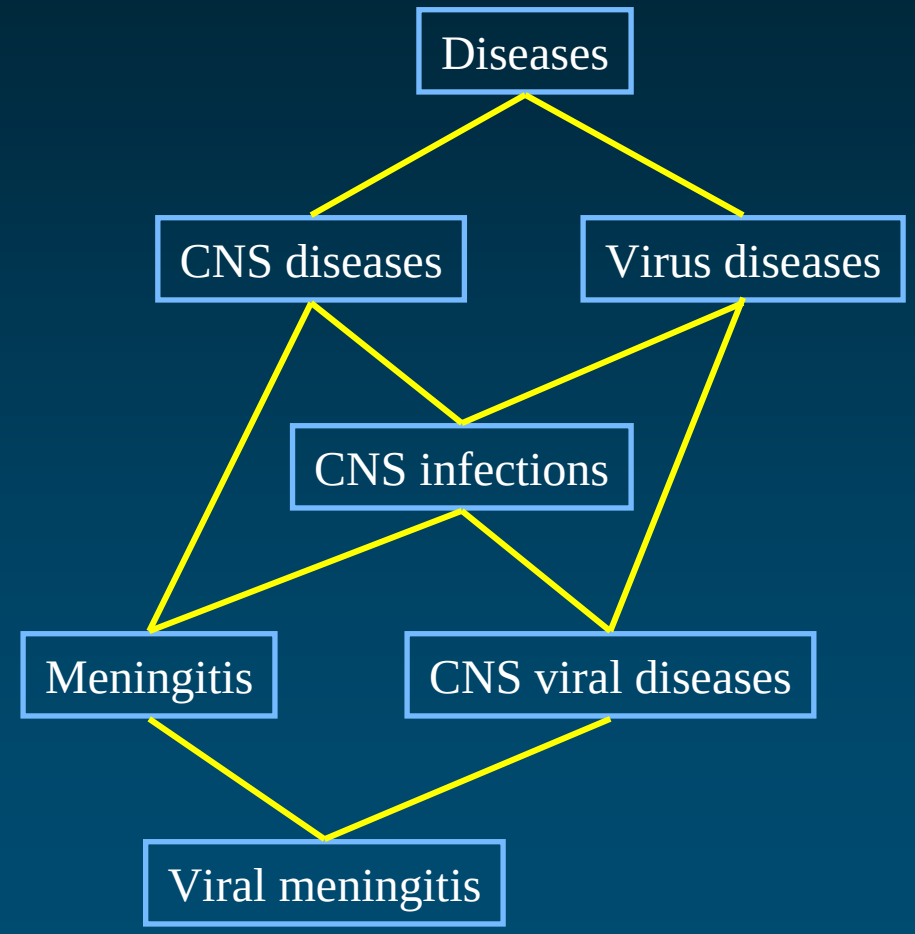
- Attribute
- Body structure
- Clinical finding
- Context-dependent categories
- Environments and geographical locations
- Events
- Observable entity
- Organism
- Pharmaceutical / biologic product
- Physical force
- Physical object
- Procedure
- Qualifier value
- Social context
- Special concept
- Specimen
- Staging and scales
- Substance

Fully specified relations

Viral meningitis in SNOMED CT



Underspecification of the relations



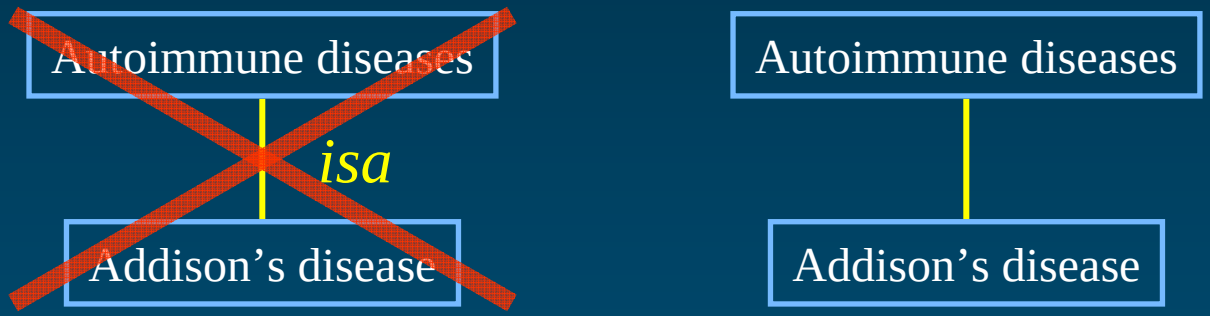
parent

isa ?

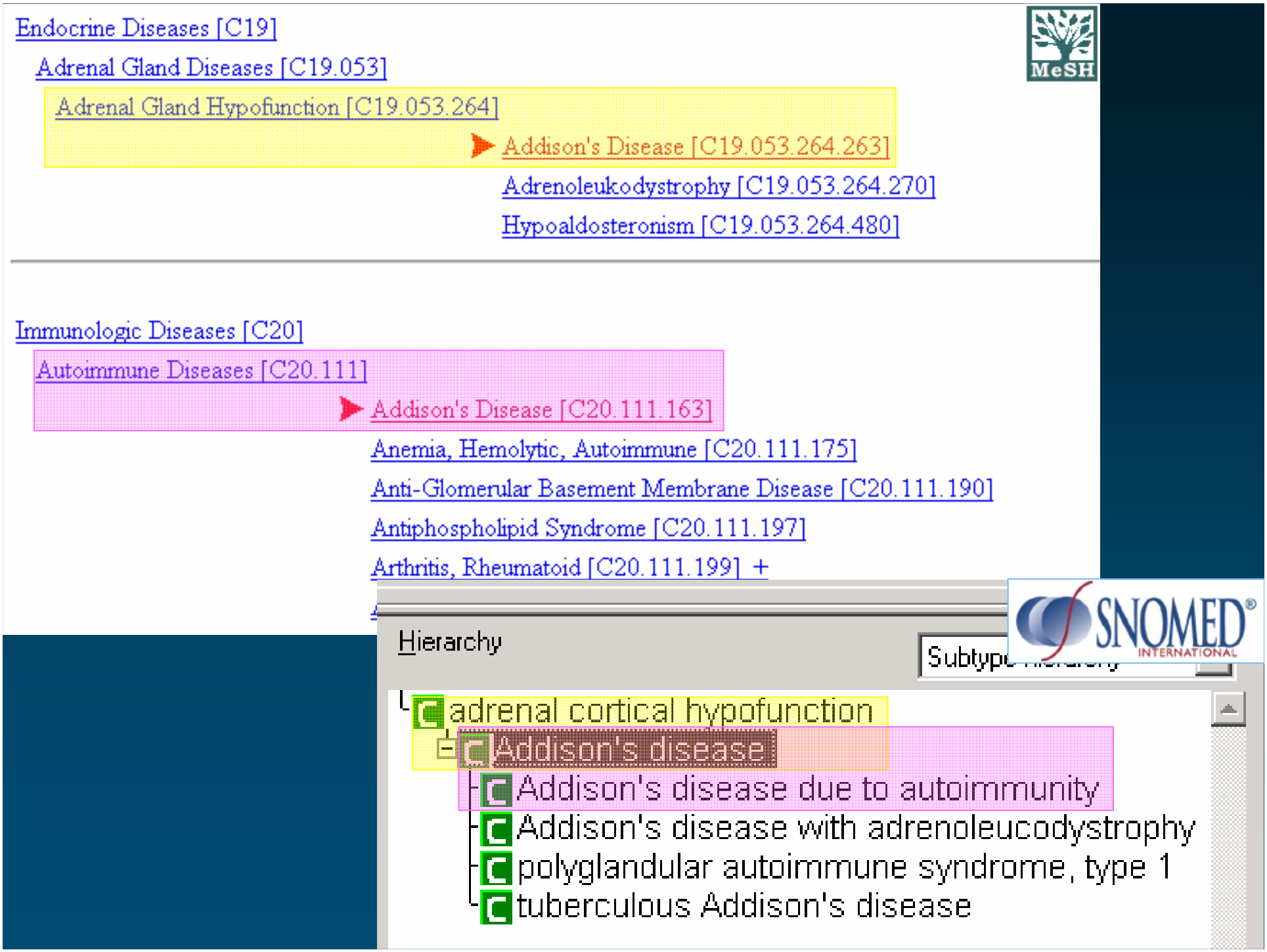
child

Thesaurus relations

- Addison's disease
  - Due to auto-immunity in 80% of the cases
  - Other causes include tuberculosis



Relations used to create hierarchical structures
vs. hierarchical relations


Endocrine Diseases [C19]
Adrenal Gland Diseases [C19.053]
Adrenal Gland Hypofunction [C19.053.264]
Addison's Disease [C19.053.264.263]
Adrenoleukodystrophy [C19.053.264.270]
Hypoaldosteronism [C19.053.264.480]
MeSH
Immunologic Diseases [C20]
Autoimmune Diseases [C20.111]
Addison's Disease [C20.111.163]
Anemia, Hemolytic, Autoimmune [C20.111.175]
Anti-Glomerular Basement Membrane Disease [C20.111.190]
Antiphospholipid Syndrome [C20.111.197]
Arthritis, Rheumatoid [C20.111.199] +
Hierarchy
adrenal cortical hypofunction
Addison's disease
Addison's disease due to autoimmunity
Addison's disease with adrenoleucodystrophy
polyglandular autoimmune syndrome, type 1
tuberculous Addison's disease
SNOMED INTERNATIONAL

Accidents in MeSH

Environment and Public Health [G03]

Public Health [G03.850]

Accidents [G03.850.110]

Accident Prevention [G03.850.110.060] +

Accidental Falls [G03.850.110.085]

Accidents, Aviation [G03.850.110.185]

Accidents, Home [G03.850.110.205]

Accidents, Occupational [G03.850.110.250] +

Accidents, Radiation [G03.850.110.285]

Accidents, Traffic [G03.850.110.320]

Drowning [G03.850.110.500] +

Limited depth in hierarchies “by design”

- Term identifier (code) used to record the position in the hierarchy
  - Limited number of digits available
  - May hide part of the structure
- Terminologies: ICD, SNOMED, …

E84 Cystic fibrosis

Includes: mucoviscidosis

E84.0 Cystic fibrosis with pulmonary manifestations

Use additional code to identify any infectious organism present, such as:
Pseudomonas (B96.5)

E84.1 Meconium ileus in cystic fibrosis

Excludes1: meconium ileus not due to Cystic fibrosis (P75)

E84.2 Cystic fibrosis with gastrointestinal manifestations

Excludes2:meconium ileus in cystic fibrosis (E84.1)

E84.8 Cystic fibrosis with other manifestations

Cystic fibrosis in ICD

E84 Cystic fibrosis

Includes: mucoviscidosis

E84.0 Cystic fibrosis with pulmonary manifestations

Use additional code to identify any infectious organism present, such as:
Pseudomonas (B96.5)

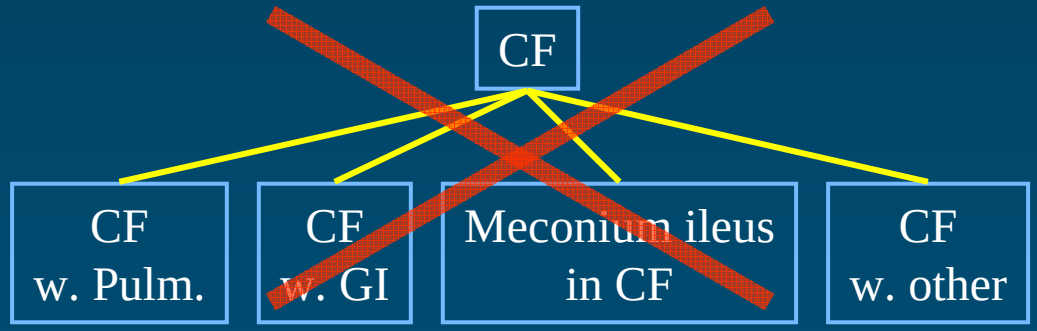
E84.1 Meconium ileus in cystic fibrosis

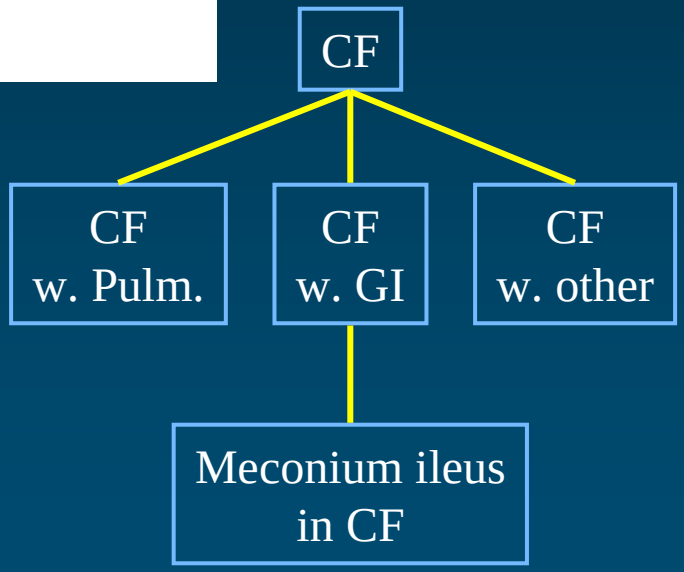
Excludes1: meconium ileus not due to Cystic fibrosis (P75)

E84.2 Cystic fibrosis with gastrointestinal manifestations

Excludes2:meconium ileus in cystic fibrosis (E84.1)

E84.8 Cystic fibrosis with other manifestations





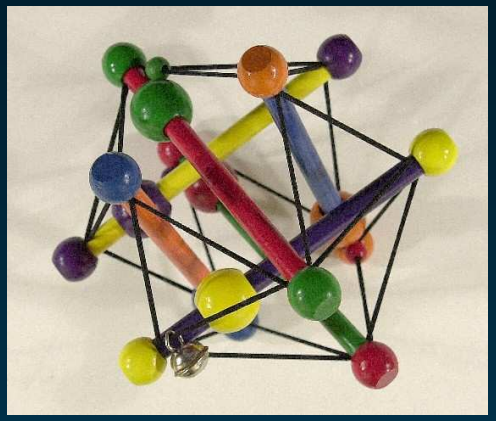
Conclusions

Conclusions ☹

- Biomedical terms
  - reflect some aspects of biomedical reality
    - Although the primary concern of terminology is naming, not reflecting reality
  - often convey additional features (e.g., epistemology)
- Biomedical terminology tends to offset part of the complexity

Conclusions ☺

- Biomedical terminologies can help populate biomedical ontologies
- Resources needed
  - Linguistic analysis of terms
  - Statistical analysis of terms in a corpus / annotation database (dependence relations)
  - Manual curation



Medical Ontology Research

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